



## A P P E N D I X I.

THE LISTING OF CLAIMS (version with markings):

1. (currently amended) An epoxide hydrolase (E.C. 3.3.2.3) from a microorganism of the genus [~~Streptomyces~~] Streptomyces.
2. (original) An epoxide hydrolase as claimed in claim 1, having at least one of the following properties:
  - a) hydrolytic epoxide cleavage of a styrene oxide and of at least one other compound selected from ethyl 3-phenylglycidates, n-hexane-1,2-oxides, n-decane-1,2-oxides and indene oxides;
  - b) conversion of a racemate of styrene oxide with an enantioselectivity  $E \geq 2$  to give (S)-phenyl-1,2-ethanol.
3. (currently amended) An epoxide hydrolase isolated from bacteria of the genus [~~Streptomyces~~] Streptomyces [~~, in particular~~] from the species [~~S. griseus~~] Streptomyces griseus, [~~S. thermovulgaris~~] Streptomyces thermovulgaris, [~~S. antibioticus~~] Streptomyces antibioticus, [~~S. arenae~~] Streptomyces arenae and [~~S. fradiae~~] Streptomyces fradiae [~~, preferably from the strains Streptomyces griseus (DSM 40236 and DSM 13447), Streptomyces thermovulgaris (DSM 40444 and DSM 13448), Streptomyces antibioticus Tü4 (DSM 12925), Streptomyces arenae Tü495 (DSM 40737 and DSM 12134) or Streptomyces fradiae Tü27 (DSM 12131)]~~].
4. (currently amended) A [~~Streptomyces antibioticus~~] Streptomyces antibioticus Tü4 deposited at the DSMZ under the Deposit Number DSM 12925.
5. (currently amended) A process for separating epoxide enantiomer mixtures, which comprises
  - a) incubating an epoxide enantiomer mixture, which comprises an epoxide hydrolase substrate, with an epoxide hydrolase as claimed in claim 1, a microorganism of the genus [~~Streptomyces~~] Streptomyces, an epoxide hydrolase-containing homogenate thereof, or a fraction of this homogenate;
  - b) converting the enantiomeric mixture [~~, preferably until the reaction equilibrium is established~~]; and
  - c) fractionating the reaction mixture.
6. (currently amended) A process as claimed in claim 5, wherein an enantiomeric mixture of an epoxide is converted, which mixture is

- selected from the group consisting of styrene oxides, 3-phenylglycidate, hexane-1,2-oxides, decane-1,2-oxides and indene oxides.
7. (currently amended) A detection method for epoxide hydrolase, which comprises
- incubating an analyte in which epoxide hydrolase activity is suspected with an epoxide-containing substrate for the hydrolase under reaction conditions, wherein the analyte is a bacterium of the genus Streptomyces, a homogenate therefrom or a fraction of this homogenate;
  - carrying out a color reaction with [~~unreacted~~] the epoxide remaining unreacted in stage a) in the presence of 4-nitrobenzylpyridine (NBP) to form a pigment; and
  - analyzing the solution from step b) for a decrease in pigment concentration, relative to an epoxide hydrolase-free control solution.
8. (original) A method as claimed in claim 7, wherein the relative decrease in pigment concentration is determined quantitatively and the epoxide hydrolase activity in the analyte is determined therefrom.
9. (canceled)
10. (canceled)
11. (currently amended) A method as claimed in claim 7, wherein the epoxide-containing substrate is selected from the group consisting of styrene oxide, 3-phenylglycidate, hexane-1,2-oxide and [~~for~~] indene oxide, each of which group members being employed in enantiomeric pure form or as an enantiomeric mixture.
12. (currently amended) A screening method for detecting microorganisms having epoxide hydrolase activity, [~~and~~] or having the ability for the enantioselective hydrolysis of epoxides, comprising a detection method as claimed in claim 7.
13. (currently amended) [~~The use of~~] A method for the enantioselective hydrolysis of epoxides, which comprises reacting an enantiomeric mixture of epoxides with an epoxide hydrolase as claimed in claim 1, a microorganism of the genus [Streptomyces] Streptomyces, an epoxide-hydrolase-containing homogenate thereof or a fraction of this homogenate [for the enantioselective hydrolysis of epoxides] to obtain a reaction mixture comprising non-reacted epoxide and a

hydroxyide, and isolating the non-reacted epoxide or the hydroxide, or both from the reaction mixture.

14. (canceled)
15. (currently amended) A process for producing epoxide hydrolases (E.C. 3.3.2.3), ~~[wherein]~~ which comprises
- a) producing a cell homogenate ~~[is produce]~~ from a culture of a microorganism of the genus ~~[Streptomyces]~~ Streptomyces;
  - b) fractionating the homogenate ~~[is fractioned]~~ obtained in stage a), and testing the resultant fractions ~~[being tested]~~ for epoxide hydrolase activity~~[, if appropriate using a detection method as claimed in claim 7]~~; and
  - c) combining fractions having epoxide hydrolase activity, ~~[are combined]~~ and ~~[if appropriate]~~ optionally further ~~[fractionated]~~ fractionating the combined fractions.
16. (new) The epoxide hydrolase of claim 3, wherein the bacteria of the genus *Streptomyces* are selected from the strains *Streptomyces griseus* (DSM 40236 and DSM 13447), *Streptomyces thermovulgaris* (DSM 40444 and DSM 13448), *Streptomyces antibioticus* Tü4 (DSM 12925), *Streptomyces arenae* Tü495 (DSM 40737 and DSM 12134) and *Streptomyces fradiae* Tü27 (DSM 12131).
17. (new) The process of claim 5, wherein the conversion of stage (b) is allowed to proceed until reaction equilibrium is established before proceeding to stage (c).
18. (new) The process of claim 15, wherein the resultant fractions are tested for epoxide hydrolase activity by a method which comprises
- a) incubating an analyte in which epoxide hydrolase activity is suspected with an epoxide-containing substrate for the hydrolase under reaction conditions, wherein the analyte is a bacterium of the genus *Streptomyces*, a homogenate therefrom or a fraction of this homogenate;
  - b) carrying out a color reaction with the epoxide remaining unreacted in stage a) in the presence of 4-nitrobenzylpyridine (NBP) to form a pigment; and
  - c) analyzing the solution from step b) for a decrease in pigment concentration, relative to an epoxide hydrolase-free control solution.

19. (new) The process of claim 18, wherein the relative decrease in pigment concentration is determined quantitatively and the epoxide hydrolase activity in the analyte is determined therefrom.
20. (new) The process of claim 18, wherein the epoxide-containing substrate is selected from the group consisting of styrene oxide, 3-phenylglycidate, hexane-1,2-oxide and indene oxide, each of which group members being employed in enantiomeric pure form or as an enantiomeric mixture.
21. (new) The process of claim 18, wherein the bacteria of the genus *Streptomyces* are selected from the strains *Streptomyces griseus* (DSM 40236 and DSM 13447), *Streptomyces thermovulgaris* (DSM 40444 and DSM 13448), *Streptomyces antibioticus* Tü4 (DSM 12925), *Streptomyces arenae* Tü495 (DSM 40737 and DSM 12134) and *Streptomyces fradiae* Tü27 (DSM 12131).

§§ 1.198 and 1.981, or to carry into effect a recommendation under § 1.196 or § 1.977.

[24 FR 10332, Dec. 22, 1959; 46 FR 29183, May 29, 1981; para. (a) revised, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997; revised, 65 FR 14865, Mar. 20, 2000, effective May 29, 2000 (adopted as final, 65 FR 50092, Aug. 16, 2000); paras. (b) and (d) revised, 65 FR 76756, Dec. 7, 2000, effective Feb. 5, 2001]

#### § 1.117 [Reserved]

[Removed and reserved, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997]

#### § 1.118 [Reserved]

[48 FR 2712, Jan. 20, 1983, effective Feb. 27, 1983; removed and reserved, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997]

#### § 1.119 [Reserved]

[32 FR 13583, Sept. 28, 1967; removed and reserved, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997]

#### § 1.121 Manner of making amendments in applications.

(a) *Amendments in applications, other than reissue applications.* Amendments in applications, other than reissue applications, are made by filing a paper, in compliance with § 1.52, directing that specified amendments be made.

(b) *Specification.* Amendments to the specification, other than the claims, computer listings (§ 1.96) and sequence listings (§ 1.825), must be made by adding, deleting or replacing a paragraph, by replacing a section, or by a substitute specification, in the manner specified in this section.

(1) *Amendment to delete, replace, or add a paragraph.* Amendments to the specification, including amendment to a section heading or the title of the invention which are considered for amendment purposes to be an amendment of a paragraph, must be made by submitting:

(i) An instruction, which unambiguously identifies the location, to delete one or more paragraphs of the specification, replace a paragraph with

one or more replacement paragraphs, or add one or more paragraphs;

(ii) The full text of any replacement paragraph with markings to show all the changes relative to the previous version of the paragraph. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strikethrough cannot be easily perceived;

(iii) The full text of any added paragraphs without any underlining; and;

(iv) The text of a paragraph to be deleted must not be presented with strike-through or placed within double brackets. The instruction to delete may identify a paragraph by its paragraph number or include a few words from the beginning, and end, of the paragraph, if needed for paragraph identification purposes.

(2) *Amendment by replacement section.* If the sections of the specification contain section headings as provided in § 1.77(b), § 1.154(b), or § 1.163(c), amendments to the specification, other than the claims, may be made by submitting:

(i) A reference to the section heading along with an instruction, which unambiguously identifies the location, to delete that section of the specification and to replace such deleted section with a replacement section; and;

(ii) A replacement section with markings to show all changes relative to the previous version of the section. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived.

(3) *Amendment by substitute specification.* The specification, other than the claims, may also be amended by submitting::

(i) An instruction to replace the specification; and

(ii) A substitute specification in compliance with §§ 1.125(b) and (c).

(4) *Reinstatement of previously deleted paragraph or section.* A previously deleted paragraph or section may be reinstated only by a subsequent amendment adding the previously deleted paragraph or section.

(5) *Presentation in subsequent amendment document.* Once a paragraph or section is amended in a first amendment document, the paragraph or section shall not be represented in a subsequent amendment document unless it is amended again or a substitute specification is provided.

(c) *Claims.* Amendments to a claim must be made by rewriting the entire claim with all changes (e.g., additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an existing claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

(1) *Claim listing.* All of the claims presented in a claim listing shall be presented in ascending numerical order. Consecutive claims having the same status of “canceled” or “not entered” may be aggregated into one statement (e.g., Claims 1–5 (canceled)). The claim listing shall commence on a separate sheet of the amendment document and the sheet(s) that contain the text of any part of the claims shall not contain any other part of the amendment.

(2) *When claim text with markings is required.* All claims being currently amended in an amendment paper shall be presented in the claim listing, indicate a status of “currently amended,” and be submitted with markings to indicate the changes that have been made relative to the immediate prior version of the claims. The text of any added subject matter must be shown by underlining the added text. The

text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. Only claims having the status of “currently amended,” or “withdrawn” if also being amended, shall include markings. If a withdrawn claim is currently amended, its status in the claim listing may be identified as “withdrawn— currently amended.”

(3) *When claim text in clean version is required.* The text of all pending claims not being currently amended shall be presented in the claim listing in clean version, i.e., without any markings in the presentation of text. The presentation of a clean version of any claim having the status of “original,” “withdrawn” or “previously presented” will constitute an assertion that it has not been changed relative to the immediate prior version, except to omit markings that may have been present in the immediate prior version of the claims of the status of “withdrawn” or “previously presented.” Any claim added by amendment must be indicated with the status of “new” and presented in clean version, i.e., without any underlining.

(4) *When claim text shall not be presented; canceling a claim.*

(i) No claim text shall be presented for any claim in the claim listing with the status of “canceled” or “not entered.”

(ii) Cancellation of a claim shall be effected by an instruction to cancel a particular claim number. Identifying the status of a claim in the claim listing as “canceled” will constitute an instruction to cancel the claim.

(5) *Reinstatement of previously canceled claim.* A claim which was previously canceled may be reinstated only by adding the claim as a “new” claim with a new claim number.

(d) *Drawings.* One or more application drawings shall be amended in the following manner: Any changes to an application drawing must be in compliance with § 1.84 and must be submitted on a replacement sheet of drawings which shall be an attachment to the amendment document and, in the header, labeled “Replacement Sheet.” Any replacement sheet of drawings shall include all of the figures appearing

on the immediate prior version of the sheet, even if only one figure is amended. All changes to the drawing(s) shall be explained, in detail, in either the drawing amendment or remarks section of the amendment paper.

(1) A marked-up copy of any amended drawing figure, including annotations indicating the changes made, may be included. The marked-up copy must be clearly labeled as “Annotated Marked-up Drawings” and must be presented in the amendment or remarks section that explains the change to the drawings.

(2) A marked-up copy of any amended drawing figure, including annotations indicating the changes made, must be provided when required by the examiner.

(e) *Disclosure consistency.* The disclosure must be amended, when required by the Office, to correct inaccuracies of description and definition, and to secure substantial correspondence between the claims, the remainder of the specification, and the drawings.

(f) *No new matter.* No amendment may introduce new matter into the disclosure of an application.

(g) *Exception for examiner’s amendments.* Changes to the specification, including the claims, of an application made by the Office in an examiner’s amendment may be made by specific instructions to insert or delete subject matter set forth in the examiner’s amendment by identifying the precise point in the specification or the claim(s) where the insertion or deletion is to be made. Compliance with paragraphs (b)(1), (b)(2), or (c) of this section is not required.

(h) *Amendment sections.* Each section of an amendment document (e.g., amendment to the claims, amendment to the specification, replacement drawings, and remarks) must begin on a separate sheet.

(i) *Amendments in reissue applications.* Any amendment to the description and claims in reissue applications must be made in accordance with § 1.173.

(j) *Amendments in reexamination proceedings.* Any proposed amendment to the description and claims in patents involved in reexamination proceedings must be made in accordance with § 1.530.

(k) *Amendments in provisional applications.* Amendments in provisional applications are not usually made. If an amendment is made to a provisional

application, however, it must comply with the provisions of this section. Any amendments to a provisional application shall be placed in the provisional application file but may not be entered.

[32 FR 13583, Sept. 28, 1967; 46 FR 29183, May 29, 1981; para. (e), 49 FR 555, Jan. 4, 1984, effective Apr. 1, 1984; revised, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997; revised, 65 FR 54604, Sept. 8, 2000, effective Nov. 7, 2000; para. (i) revised, 65 FR 76756, Dec. 7, 2000, effective Feb. 5, 2001; revised, 68 FR 38611, June 30, 2003, effective July 30, 2003]

## § 1.122 [Reserved]

[24 FR 10332, Dec. 22, 1959; para. (b), 49 FR 48416, Dec. 12, 1984, effective Feb. 11, 1985; removed and reserved, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997]

## § 1.123 [Reserved]

[48 FR 2712, Jan. 20, 1983, effective Feb. 27, 1983; 49 FR 555, Jan. 4, 1984, effective Apr. 1, 1984; amended, 58 FR 38719, July 20, 1993, effective Oct. 1, 1993; removed and reserved, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997]

## § 1.124 [Reserved]

[Removed and reserved, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997]

## § 1.125 Substitute specification.

(a) If the number or nature of the amendments or the legibility of the application papers renders it difficult to consider the application, or to arrange the papers for printing or copying, the Office may require the entire specification, including the claims, or any part thereof, be rewritten.

(b) Subject to § 1.312, a substitute specification, excluding the claims, may be filed at any point up to payment of the issue fee if it is accompanied by a statement that the substitute specification includes no new matter.

(c) A substitute specification submitted under this section must be submitted with markings showing all the changes relative to the immediate prior version of the specification of record. The text of any added subject matter must be shown by underlining the